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Title: A Diagnosis of Endometrial Hyperplasia: Where are we now?

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Purpose:

Endometrial hyperplasia (EH) is an 'umbrella-term' depicting a heterogeneous collection of morphologically abnormal endometrial lesions. When cytological atypia is present there is substantial risk of endometrioid endometrial cancer development. In 2014, the WHO endorsed the Endometrial Intraepithelial Neoplasia (EIN) system of EH classification. Although predominantly a morphological classification, it recognises the importance of unopposed oestrogen stimulation in EH development, distinguishing it from a mutationally activated premalignant clone (EIN) developing in an oestrogen stimulated background. Utilising EIN criteria has been shown to increase diagnostic reproducibility and aligns well with clinical treatments, more so than the preceding WHO94 classification.

Methods:

Pathology reports coded as EH using WHO94 diagnostic criteria within NHS Lothian were retrospectively evaluated from 2004-2009. The index diagnostic sections (n=127) underwent blinded expert gynae-path review to: 1) verify WHO94 diagnosis and 2) reclassify using EIN criteria. FFPE sections were obtained from the cohort (LREC:15/ES/0094) and immunohistochemistry performed (PTEN, PAX2, ARID1A, HAND2, p53) for characterisation of molecular features.

Results:

Agreement between initial WHO94 diagnosis and expert review WHO94 diagnosis was 52% (n=66). The largest inconsistency was within the WHO94 complex EH category, where only 38.5% (10/26) of review diagnoses agreed with the original. The cohort contained 44 EIN and 83 non-EIN cases. Of note, PTEN-null gland expression was found in 56.8% (25/44) of EIN cases, including 38.6% (17/44) where the entire EIN lesion was PTEN-null.

Conclusions:

Our study highlights problematic interobserver differences encountered using WHO94, which remains a familiar system in gynaecological practice, thus creating potential for under/overtreatment of EH. Work continues to fully elucidate the molecular features of EH/EIN and unravel underlying neoplastic mechanisms.